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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,405	11/21/2001	Alan L. Mueller	072827-1905	4028
23620	7590	06/01/2005	EXAMINER	
FOLEY & LARDNER 402 WEST BROADWAY 23RD FLOOR SAN DIEGO, CA 92101			KWON, BRIAN YONG S	
			ART UNIT	PAPER NUMBER
			1614	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/990,405	Applicant(s) MUELLER ET AL	
	Examiner Brian S. Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,6 and 21-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,6 and 21-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of Application

1. The rejection of the claims 5-6 and 21-24 under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (Journal of Medicinal Chemistry, 1971, Vol. 14, No.2, pp. 161-4) is maintained for the reasons of record.
2. Claims 5-6 and 21-24 are currently pending for prosecution of the merits.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

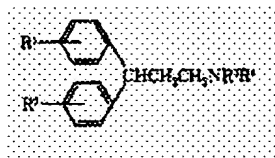
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 5-6 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (Journal of Medicinal Chemistry, 1971, Vol. 14, No.2, pp. 161-4).



Jones teaches use of 1,1-diphenyl-3-aminopropanes, wherein R1 is H, 3-F, 3-CF3, 2-Me, 2-MeO, 4-F, 4-Cl; R2 is H, 3-F, 3-CF3, 4-F, 4-Cl; R3 is CH3; R4 is H or CH3; or pharmaceutically acceptable salts (e.g., HCl, oxalate), as antidepressant agent that is useful for the treatment of depression (Table III; Experimental Section in pages 162-163).

The teaching of Jones differs from the prior art by reciting a specific species, more particularly 3-F at X 1 and X2 and -CH3 or -H at R3 (claims 22 and 24). However, it would have been obvious to a person skilled in the art at the time of the invention was made to arrive at the claimed invention since an ordinary skill in the art would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as the genus as a whole. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Response to Arguments

4. Applicant's arguments filed March 22, 2005 have been fully considered but they are not persuasive.

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Applicant's argument in the response takes the position that Jones reference does not teach or suggest to make any modifications to the compounds disclosed in Table III, or any advantages that any such modifications might have. Applicant alleges that there would be no motivation for the skilled artisan to select the saturated compounds of Table III since the activities of all of the compounds Table III, which shows saturated compounds corresponding to "generic structure V" (i.e., the olefinic series), are less active than the activities of the six compounds (compound 5, 6, 15, 16, 17 and 18) that are demonstrated to be comparable with those of known clinically effective antidepressants or more active in the pharmacological and biochemical tests reported.

Applicant's argument is found unpersuasive. Jones discloses that the potential antidepressant activity of the test compounds is assessed by their ability to antagonize reserpine-induced hypothermia in mice. In Table I, the reversal of reserpine-induced hypothermia values for amitriptyline, imipramine, desipramine and nortriptyline are expressed as 3, 7, 0.8-1.6 and 1.0-2.0, respectively. In other words, compounds of the Jones having ranges of reversal of reserpine-induced hypothermia value between 0.8 and 7 are generally considered to have the potential antidepressant activity. Looking at the Table I and Table III of the Jones, it is clear that compounds having halogen substituent(s), especially F or Cl, in the Ph rings and Me or two Me radicals substituent(s) at N demonstrate comparable or better antidepressant activity as the known antidepressants (i.e., amitriptyline, imipramine, desipramine and nortriptyline). For example, Compound 51 (where R1 and R2 is independently 3-F and R3 and R4 is independently CH3) in Table III, similarly to the Compounds 28 and 29 (where R1 and R2 is independent 3-F and R3 and R4 is independently CH3 or H) in Table I, shows the reversal of reserpine induced

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hypothermia value of 2. Thus, one having ordinary skill in the art would have expected as taught by the Compounds 28 and 29 that substitution of H at R4 for CH3 would not alter the analogous properties of the Compounds 51 of the Jones due to close structural similarity of the compounds.

Applicant's argument in the response takes the position that one of ordinary skill in the art would not have a reasonable basis to accurately predict whether any particular modification would result in a beneficial effect, a negative effect or no effect at all on the biological activity of the compound since the data provided in Table III shows that variations in the structure of the compounds significantly affects the properties of the compounds with respect to their performance in the indicated assays.

Applicant's argument is found unpersuasive. Although compounds disclosed in Table III show some variations in their potential antidepressant activity depending upon different substituents at R1, R2, R3 and R4, there is no doubt that substitution in the Ph rings with halogen, especially F or Cl, and substitution in N with CH3 and/or H preserves the antidepressant activity of the compounds. As discussed above, the Compound 28, 29 and 51 show similar antidepressant activity. One having ordinary skill in the art would have been motivated to select the claimed compound(s) with the reasonable expectation of success that substitution of H at R4 for CH3 would not alter the analogous properties of the Compounds 51 of the Jones due to close structural similarity of the compounds. Furthermore, one having ordinary skill in the art would have expected that substitution of other halogen (i.e., 3-Cl and 3-Br) for 3-F at R1 and R2 position would not alter the analogous properties of the Compounds of 28, 29 and 51 due to close structural similarity of the compounds.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

6. No Claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.


CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

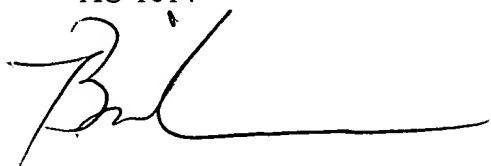
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Brian Kwon
Patent Examiner

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A handwritten signature in black ink, appearing to be 'Brian Kwon', with a long horizontal stroke extending to the right.